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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,712	12/12/2000	D. Wade Walke	LEX-0109-USA	5587

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/735,712	WALKE ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RL

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 01/28/2005 has been entered in full. Claims 1-9 are currently pending and under consideration.

Claim rejection under 35 U.S.C. § 101

The rejection of claims 1-9 under 35 U.S.C. §101 is maintained. Claims 1-9 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well-established utility. The basis for this rejection is set forth in the previous Office Actions (Paper No. 9, 12, 18, 21, and 08132004).

Beginning at page 2 of Applicants' response, Applicants cite USPTO's Utility Examination Guidelines, case law, and review the legal standard for utility, with which the Examiner takes no issue.

From the bottom of page 3 to top of page 4 of the Applicants' response, Applicants argue that the specification asserted that the sequences of the present invention encode novel human membrane proteins that shares sequence and structural similarity with mammalian CD20 protein and that such membrane receptor proteins play a role in

the activation and release of agents that mediate a variety of allergic and inflammatory reactions. Applicants further submit that the specification describes the association of a person with a mutation in the sequences of the present invention manifesting the phenotypes of, among others, connective tissue disorders. Applicants submit that Applicants have asserted that the protein encoded by the sequence of the present invention play a biological role in both immune function and connective tissue disorders.

This has been fully considered but is not deemed to be persuasive for the following reasons. As noted in previous office actions (paper No. 9, 12, and 21), sequence homology with human CD20 antigen or other sequences present in databases does not render the present sequences a specific biological function or physiological significance because the state of the art in protein science indicates that it is impossible to predict protein functions solely based upon sequence homology. While CD20 antigen-like proteins may be structurally related as Applicants argued, no single specific biological function or activity has been assigned to the protein family. As stated by Ishibashi et al., "The identification of this relatively large gene family in various tissues will allow the further elucidation of physiological significance of this gene family, that is currently unclear." (Gene, 264: 87-93, 2001). The Examiner's position is further supported by the fact that the CD20 knockout mouse cited in Nature Review Drug Discovery exerted the phenotype of depletion of a subpopulation of B cells, whereas the present knockout mouse showed an increased level of NK cells, even though Applicants assert that the protein of the present invention is CD20 antigen-like. Therefore, the sequence

homology alone does not provide a specific and substantial utility for the present sequences.

Moreover, the instant specification fails to provide a specific and substantial utility for the claimed invention. The specification asserts that the human membrane proteins of the present invention shares structural similarity with membrane receptors such as, but not limited to, the IgE receptor and mammalian CD20 (top of page 2). At page 12 of the specification, Applicants assert that a genomic library can be constructed using DNA obtained from an individual suspected of or known to carry a mutant NHP allele (e.g., a person manifesting a NHP-associated phenotype such as, for example, obesity, high blood pressure, connective tissue disorders, infertility, etc.). Clearly, further experimentation is required to identify the specific biological functions of the polypeptides encoded by the present nucleic acid molecules.

At the 2nd paragraph of page 4 of the Applicants' response, Applicants argue that the amino acid sequence of SEQ ID NO: 2 of the present invention are identical to Accession No. Q9H3V2, which has been annotated as encoding "Membrane-spanning 4-domains subfamily A member 5 (testis-expressed transmembrane 4 protein)(CD20 antigen-like 2)". Applicants further submit that clearly those of skill in the art would find Applicants' identification of the structural identity of the protein encoded by the sequences of he present invention as credible, since the same assertions have been made by several other third party scientists unaffiliated with Applicants.

This has been fully considered but is not deemed to be persuasive for the following reasons. First, while sharing sequence homology, SEQ ID NO: 2 of the present invention is NOT identical to Accession No. Q9H3V2. As noted above, the sequence homology alone does not render the present sequence a patentable utility. Secondly, the cited publications do not identify a specific biological function or any physiological significance for the present sequence; these studies are also based upon sequence analysis. As stated by Ishibashi et al., "The identification of this relatively large gene family in various tissues will allow the further elucidation of physiological significance of this gene family, that is currently unclear." (Gene, 264: 87-93, 2001). Therefore, the cited references do not provide a specific and substantial utility for the present sequences.

From the bottom of page 4 to top of page 4 of the Applicants' response, Applicants argue that disruption of the mouse ortholog of the claimed human sequences and thus elimination of the encoded protein resulted in an increase in the level of natural killer (NK) cells in the blood. Applicants submit that the declaration under 37 C.F.R. § 1.132 by Dr. Oravecz clearly indicates that the protein encoded by the murine ortholog of the human sequences of the present invention plays a role in NK cell regulation and is associated with connective tissue disorders.

This has been fully considered but is not deemed to be persuasive because there is no support for such a regulatory role of the protein of the present invention in NK cell level in the application as originally filed; nowhere does the specification disclose that the nucleic acid and/or protein have any links with the NK cell levels. Therefore, the Applicants were not in possession of the utility at the time when the application was filed.

Beginning at the bottom of page 5 of the Applicants' response, Applicants criticizes the Examiner's position that it is impossible to predict protein functions based solely upon sequence homology. Applicants argue, citing Example 10 of the Revised Interim Utility guidelines Training materials, that even the USPTO accepts that there is a structure/function relationship when a high degree if homology exists between a full length sequence and a protein having a known function.

This has been fully considered but is not deemed to be persuasive. In Example 10 of the Revised interim Utility Guidelines Training Materials, the claimed nucleic acid sequence has a well-established utility because the high sequence homology can place the protein encoded by the claimed nucleic acid sequence in a DNA ligase family, whereas ligases have a well-established use in ligating DNA. It is not the case here. Moreover, the degree of homology that the proteins encoded by the claimed nucleic acid molecules share with CD20 is not disclosed. Furthermore, no single specific biological function or activity has been assigned to the CD20 protein family. As stated

by Ishibashi et al., "The identification of this relatively large gene family in various tissues will allow the further elucidation of physiological significance of this gene family, that is currently unclear." (Gene, 264: 87-93, 2001).

Beginning at the bottom of page 5 of the Applicants' response, Applicants argue that the Examiner erroneously equates CD20 and its respective knockout mouse and findings submitted in regard to the instant case with the CD20-like molecules encoded by the sequence of the present invention. Applicants submit that they have never asserted that the sequence of the present invention encode CD20 but rather that they encode a protein that is CD20-like. This is not found persuasive because Applicants' argument is based upon ill reasoning: on one hand, Applicants argue that the proteins of the present invention are "CD20-like" molecules; on the other hand, they argue that the proteins of the present invnetion do not act like CD20.

Beginning at the 4th paragraph of page 6 of the Applicants' response, Applicants criticizes the Examiner's position and argue that if the absence of the CD20-like molecule encoded by the sequences of the present invention in the knockout mouse results in increased NK cell levels, then one would reasonably anticipate that increased levels of this molecule would have the opposite effect and lower the levels of NK cells. Applicants also criticizes the Examiner's statement that Applicants' knockout mouse study does not show, by any means, that there is a causative link between the protein encoded by the claimed nucleic acid sequences and a connective tissue disorder.

Applicants submit that the Examiner's statement is totally irrelevant to the present discussion and clearly emphasizes the improper standard for utility that many Examiners have adopted. Applicants submit that the issue under 35 U.S.C. §101 is not one of a causative human disease link but simple a credible, specific, and substantial asserted utility or a well-established utility.

This has been fully considered but is not deemed to be persuasive. First and foremost, there is no support for such a regulatory role of the protein of the present invention in NK cell level in the application as originally filed; nowhere does the specification disclose that the nucleic acid and/or protein have any links with the NK cell levels. Therefore, Applicants were not in possession of the utility at the time when the application was filed. Secondly, a causative link between the protein encoded by the claimed nucleic acid sequences and a connective tissue disorder is necessary for establishment of a role of the proteins encoded by the claimed nucleic acids in a connective tissue disorder, as applicants have argued. Moreover, there is no evidence supporting applicants' argument that increased levels of this molecule would have the opposite effect and lower the levels of NK cells.

Beginning at the third paragraph of page 7 of Applicants' response, Applicants summarize their arguments and submit that as asserted in the specification as filed, the novel human membrane proteins encoded by the sequences of the present invention play a role in inflammatory reactions and that a mutation in the sequences of the

present invention can manifest itself as a connective tissue disorder. Those of skill in the art would clearly recognize the utility of the present invention. Applicants submit that the present invention is in full compliance with the provisions of 35 U.S.C. 101.

This has been fully considered but is not deemed to be persuasive for the reasons set forth above and in the previous office actions.

In summary, the specification fails to provide a specific, substantial, and credible utility, or a well-established utility for the claimed invention.

Claim Rejections Under 35 U. S. C. § 112, 1st Paragraph

The rejection of claims 1-9 under 35 U.S.C. §112, 1st Paragraph due to lack of utility is maintained. Since the claimed invention is not supported by either a specific, substantial, and credible utility, or a well-established utility, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth in the previous Office Actions (Paper No. 9, 12, 18, 21, and 08132004).

Applicants' argument about the patentable utility of the claimed invention has been fully considered but is not deemed to be persuasive for the reasons set forth above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Examiner
April 7, 2005